Pain and Disability scales were used to quantify pain and disability. Catastrophizing was measured with the Pain Catastrophizing Scale. Repeated measures general linear models were used to compare the patients in the treatment group to a usual care cohort of 45 patients who also had received knee arthroplasty and had high pain catastrophizing but no pain coping skills training. Patient groups has comparable baseline characteristics.
Results: Compared to the usual care cohort, the patients who received pain coping skills training reported significantly greater and clinically important reductions in pain severity and catastrophizing, and greater improvements in function, two months after surgery (see table).
Conclusions: The findings provide preliminary evidence that the pain coping skills treatment may be highly efficacious for reducing pain, catastrophizing, and disability, in patients reporting elevated catastrophizing prior to knee arthroplasty. A randomized clinical trial is warranted to confirm these effects.

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PERSISTENT KNEE PAIN AFTER A KNEE REPLACEMENT FOR OSTEOARTHRITIS

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Purpose: Knee joint replacement is a successful, effective and cost effective procedure for the treatment of osteoarthritis (OA). However, there are a small number of patients who complain of persistent pain in the operated joint, in spite of an apparently good technical outcome.
This study is a preliminary investigation into the causes of persistent pain in the operated knee after technically successful medial uni-compartmental knee joint replacement for antero-medial knee OA.
Methods: People with persistent knee pain of no known cause, and a duration of 6 months or more after medial compartment UKR for OA, were invited to attend a special clinic where a full history was taken, and examination including quantitative sensory testing carried out. 21 subjects agreed to attend.
Results: 18 of the 21 patients were women (compared with a F:M ratio of 1.1:1 for all UKRs done in the unit), their mean age was 58 (range 43-69) and the mean interval since operation was 13 months (range 6 months to 3.5 years). Their current pain was described as severe by 10, moderate in 9 and mild in 1 case. 16 of the 21 subjects described the pain as quite different in quality from the arthritis pain that they had experienced prior to surgery, and 10 people described transient sharp attacks of spontaneous pain in addition to their 'usual' more constant pain. On the basis of the history and examination, patients were divided into three overlapping groups:
1. *Neuropathic pain:* Sensory testing revealed allodynia in 10 cases, which was severe in 7 and associated with a high score on 'PainDetect' questionnaires.
2. *Mechanical pain:* This group (n=7) complained of pain which was either similar to that prior to surgery (5) and/or clearly associated with activity. Examination suggested that the pain was coming from other compartments of the knee, (e.g. patello-femoral joint), or from periarticular soft tissues.
3. *Infero-medial bone pain:* This group of another 7 patients complained of a new sort of pain developing post-operatively, characterised by a dull ache radiating down the medial side of the tibia, unrelated to activity.
In 5 cases there appeared to be a mixture of features, including aspects of two or more of the above categories
Conclusions: Pain in OA joints with technically successful prostheses is not uncommon and has a number of different causes. In the case of UKR, a specific syndrome of antero-medial 'bone' pain can develop, in addition to mechanical or neuropathic pain. These different types of pain can be distinguished in clinic, and require different therapeutic approaches.

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THE IMPACT OF INVESTIGATIONAL SITE QUALITY TO PROVE EFFECTS ON PAIN IN CLINICAL STUDIES OF OSTEOARTHRITIS OF THE KNEE

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Purpose: Failure of large interventional, controlled studies in osteoarthritis (OA) is not uncommon. If a study includes an internal control ("gold standard"), reasons other than failure of the experimental drug can be explored. Poor study conduct at investigational sites is one of the reasons why a study may fail. We explored and exemplified the problem using two large multicenter phase III studies with similar design and inclusion/exclusion criteria investigating Diractin® (Ketoprofen Transfersome® Gel). Whereas Study 1 showed statistically significant results on pain, Study 2 failed to confirm those in the primary data analysis.
Methods: *Study 1* was a multi-center, randomized, double-blind, multiple dose, parallel group, placebo-controlled study investigating three different dosages of ketoprofen in Diractin® in patients with OA of the knee (100 mg bid [n=223], 50 mg bid [n=223], 25 mg bid [n=221] and placebo [n=199]) for a treatment period of 12 weeks. *Study 2* was a multi-center, randomized, double-blind, double-dummy, multiple dose, parallel group, placebo- *and* active (naproxen)-controlled study investigating Diractin® in the same dosages (100 mg bid [n = 164], 50 mg bid [n = 172], and 25 mg bid [n = 175]), naproxen 500 mg bid [n = 164] and placebo [n = 162] for 12 weeks. Both studies used the VAS version of the WOMAC pain subscale to evaluate effects on pain. Due to the high dropout rate of study 2 and the weak response of the reference drug, the concept of "quality sites" was introduced. A "quality site" was defined by: 1) at least one patient per treatment group received study medication, and 2) less than 50% major protocol violations observed. The difference in study outcome for "quality" and "non-quality sites" was evaluated using standard statistical methods for the comparison of the placebo group to the naproxen group.
Results: In Study 1, 100 mg bid and 50 mg bid of ketoprofen in Diractin® showed statistically significant effects on pain ($p = 0.0383$ and $p = 0.0204$, resp.). However, the primary analysis of Study 2 failed to show a statistically significant effect for Diractin®. The following differences between Study 1 and Study 2 were observed with respect to study conduct.

Table 1. Key conduct features of the clinical studies

	# Randomised Patients/Site	# Per Protocol Patients per Site	Drop-out Rate	Screening failure Rate
Study 1	28.0	21.0	17%	27%
Study 2	9.3	6.1	42%	92%

If the concept of "quality and non-quality sites" was introduced for Study 2, the statistical comparison of naproxen vs. placebo showed $p = 0.0005$ for the "quality sites" as compared to $p = 0.3679$ for the "non-quality sites".
Conclusions: Study conduct at the investigational site is crucial to detect therapeutic effects on pain during interventional studies in OA of the knee.

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THE CHECK COHORT: PROGRESSION OF PAIN OVER 2 YEARS OF PATIENTS SUSPECTED OF HAVING EARLY OA

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Purpose: The aim was to study the early progression of pain of patients with both hip and knee complaints over 2 years. We planned on using three different models in order to identify factors associated with progression of pain and to assess what strategy we should use to investigate changes in complaints due to (early) osteoarthritis.
Methods: A prospective cohort of 1002 participants with complaints of knee and/or hip was formed between October '02 and September '05. The participants will be followed for a period of at least 10 years.
Individuals were eligible to participate in the study if they had pain and/or stiffness of knee and/or hip, were aged between 45 and 65 years, and had never of or not longer than 6 months ago visited the GP for these symptoms for the first time. Exclusion criteria were any other pathological condition that could explain the existing symptoms.
The primary outcome measures of this study were change in the Western Ontario MacMaster questionnaire (WOMAC) pain subscale from baseline to two years follow up.
Determinants were factors from the baseline assessment including: demographic factors, factors relating to symptoms, co morbidities and interventions, measurements from a physical examination, factors relating to participation and lifestyle, radiographic assessments, and psychological factors.
A univariate analysis was done on the 47 variables that were deemed relevant. The variables that were related to the outcome ($p<0.20$) were

then analysed per block. The final model was made using the enter method ($p<0.05$).
The data was analysed using 3 different approaches to define progression: 1) a change of more than 0.5 SD of the mean WOMAC pain score at baseline, 2) a shift to a higher quintile-group, or remaining in the 3 highest quintiles of WOMAC pain scores as proposed by Sharma et al., 3) any deterioration in WOMAC pain score. The first 2 approaches were analysed with logistic regression analyses. The third approach was analysed with linear regression analyses.
Results: Of the 1002 patients in the CHECK cohort, the majority were female (79%). Mean age was 56 years. 82.7% of all patients had knee pain, while 58.7% had hip pain at baseline. Almost half of the patients (41.4%) consulted for hip and knee pain.
On average the pain of the CHECK patients declined slightly over the first two years. However, after two years 40.1% of the patients had a higher WOMAC pain score than at baseline.
For the approach based on change >0.5 SD we found for hip complaints that moderate alcohol use and a higher WOMAC pain score at baseline protected against an increase, while a painful hip flexion led to more pain after two years. While the Sharma method only found a relation between a painful hip flexion and more pain. The linear regression analysis yielded that having paid employment and more pain at baseline (WOMAC) and a better health (SF 36) protected against more pain, while having concomitant complaints of arm, neck and shoulder led to more pain.
For knee complaints the SD method yielded that moderate alcohol use, more pain at baseline and a better vitality (SF 36) protected against an increase in pain, while hip stiffness and a Kellgren & Lawrence (KL) score of 2 or more was related to more pain after two years. Using the Sharma method we found that moderate alcohol use and a better physical functioning score (SF 36) protected against more pain, while hip stiffness and a KL $\geq$ 2 led to more pain after two years. Finally the linear regression showed that more pain at baseline (WOMAC) and a better physical functioning score (SF 36) protected against an increase in pain.
Conclusions: We were able to identify several predictors on progression of pain in early osteoarthritis. However the predictors for the 3 definitions of deterioration of pain are very different. Not one factor was found in all 3 methods for one joint. This indicates that the choice of what is regarded as deterioration is essential.

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NEUROMUSCULAR FUNCTION OF THE SCAPULAR STABILIZING MUSCLES WITH AND WITHOUT ELECTROMYOGRAFICAL BIOFEEDBACK

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Purpose: Subacromial impingement SI and glenohumeral osteoarthritis (OA) are traditionally treated as separate pathologic conditions but often present concurrently in the same patient and both conditions have been associated with abnormal scapular positioning and muscle coordination. A proposed impairment model could be that a lack of stabilizing activity in the lower trapezius muscle could cause an alignment deviation of the scapula. This could potentially lead to structural and pathomechanical alterations like SI as a first sign of increased deterioration in the joint eventually leading to OA. In the present study the aim was to compare subjects with SI with healthy subjects regarding the neuromuscular function during a standardized selective activation task subsequent to a visual biofeedback guided training session.
Methods: Thirty subjects volunteered, 15 subjects with impingement syndrome (40 yrs ± 13) (*imp*) and 15 healthy subjects (39 yrs ± 12) (*no-imp*). Inclusion criteria for *imp* were at least 30 days with pain/discomfort in the shoulder/neck region within the last year and 2 or more positive impingement tests, while for *no-imp* it was less than 8 days with pain/discomfort within the last year and no positive impingement tests.
Surface EMG was recorded from 4 parts of the trapezius muscle, maximal EMG amplitude (MVE) was measured and muscle activity was calculated as %MVE for each part. With subjects lying prone the EMG signals from the 4 parts of trapezius muscle were used for visual biofeedback source. Training sessions of selective activation tasks of each of the 4 parts of trapezius were conducted. Subsequently, the final task was in 3 attempts of 30 sec to perform the selective activation without visual biofeedback. Successful selective activation was defined as activity in the requested subdivision above 12% while the others were below 1.5% MVE. Secondly, during the attempt of selective activation the activation ratio was calculated as the activity of the requested muscle part relative to the total activation in all 4 muscle parts in 1 sec time bins. For each task the largest 1 sec value was taken as the peak value. An unpaired t-test was applied to test differences between groups.
Results: A significantly lower activation ratio for both the lower and upper parts was found for both *imp* and *no-imp* when no visual guiding were provided compared to the biofeedback training trials (table 1). Without feedback no subjects were able to selectively activate the upper part but 5 *no-imp* vs. 0 *imp* subjects attained selective activation of the lower part. Regarding activation ratio, there was no difference in the mean peak values of *imp* and *no-imp*. However, 9 *no-imp* vs. 3 *imp*, attained an activation ratio higher than 95% of the lower part while for the upper part none of the subjects reached 95%.

Table 1. Number (%, SD) of subjects with (imp) and without Impingement (no-imp) who are able to selectively activate trapezius muscles (upper/lower parts) during sessions with and without visual biofeedback

Subjects	N=30	Selective activation with biofeedback (%, SD)	Selective activation without biofeedback (%, SD)	Difference between selective activation with/without biofeedback (p-value)
Imp. group	15			
Lower subdivisons		95.6% (5.6)	90.5% (6.2)	($p\leq0.05$)
Upper subdivisons		85.7% (14.9)	67.5% (14.9)	($p\leq0.001$)
No-imp. group	15			
Lower subdivisions		96.4% (2.8)	93.4% (4.4)	($p\leq0.05$)
Upper subdivisions		85.3% (13.0)	70.2% (14.3)	($p\leq0.001$)

Conclusions: The results indicate that the *no-imp* subjects after a biofeedback training session have a superior scapula muscle control compared to the *imp*. The observed effect of biofeedback to increase activation ratio of both upper and lower parts in attempted selective activation shows that it is feasible to use biofeedback to improve the neuromuscular function and thereby improve scapular coordination also in individuals with SI.

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HEALTH STATUS AND IMPACT OF PAIN: A COMPARATIVE STUDY BETWEEN FEMALE PATIENTS WITH THE EHLERS-DANLOS SYNDROME, FIBROMYALGIA AND RHEUMATOID ARTHRITIS

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Purpose: The Ehlers-Danlos Syndrome (EDS) is one the most prevalent heritable connective tissue disorders. Generalized severe joint hypermobility, which is frequently associated with joint dislocations, chronic pain and premature osteoarthritis, is the dominant clinical manifestation of the hypermobility subtype of EDS (EDS-HT). The musculoskeletal pain is early in onset, chronic and debilitating. However, research on the burden of the disease is scarce. The goal of this study was to compare the impact of disease, assessed by measures of pain and health-related quality of life (HRQOL), between patients with EDS-HT, fibromyalgia (FM) and rheumatoid arthritis (RA), diseases which are characterized by chronic widespread musculoskeletal pain.
Methods: A total of 206 female patients were compared: 72 patients with EDS-HT, 69 patients with FM and 65 patients with RA. The psychosocial impact of chronic pain was assessed using the Multidimensional Pain Inventory (MPI), which comprises five subscales: pain severity, pain interference, perceived life control, affective distress and social support. The health-related dysfunction was quantified using the Sickness Impact Profile (SIP), containing twelve different subscales aggregated into a physical, psychosocial and overall health dimension. Scores were compared by multivariate analysis of covariance, adjusting for age, years of education, living status, and current statute. Bonferroni's procedure was used to adjust for multiple testing.
Results: The results of this study showed an important impact of pain on everyday life for all groups (Figure 1). The MPI T-scores revealed that the EDS-HT group has significantly higher levels of pain intensity